REMARKS

By this amendment, claim 1 is amended to clarify that a primary immunocyte is explicitly recited. Claims 1-14 are pending. Support for this clarification can be found in the application as filed, for example, at page 3, lines 15 -23 as copied below. No issue of new matter arises.

> Because known vectors for pathway mapping of immunocytes are not efficient enough to be practical for use on primary immunocytes, pathway mapping using methods of the prior art can currently only be performed on cultured cell lines. However, immortalized cultured cell lines tend to have a significantly different patterns of protein expression than their non-immortalized counterparts. It is desirable to be able to perform pathway mapping on primary host cells of higher organisms without unnecessarily disrupting their cells' normal pattern of expression. It is especially desirable to be able to perform pathway mapping on primary immunocytes without having to transform them into immortal cell lines.

Rejection under 35 U.S.C. §103(a)

Claims 1, 5 and 8-10 were rejected under 35 U.S.C. 103(a) as allegedly "being unpatentable over *Chanda et al.* (USP 7,344,833), in view of *Kikuchi et al.* (J Antimicrobial Chemother 2002;49:745-55) and *Kraal et al.* (J Exp Med 1986;163:981-97)."

The Office Action explained the rejection as follows:

> *Chanda* teaches methods for screening modulators of AP-1 transcription factor activities in a cell (e.g. the abstract). *Chanda* teaches AP-1 protein is normally expressed by lymphoid cells (immunocyte) and induces macrophage (immunocyte) phagocytosis and activation, and induces hematopoietic progenitor cell (immature dendritic cell) differentiation (e.g. column 1, lines 41-50). *Chanda* teaches when using cell-based assays, the steps for the screening include introducing into appropriate host cells vectors expressing a reporter gene and linked to the coding sequence of an AP-1 subunit under the control of an AP-1 transcription regulatory element (promoter and enhancer sequence); and activities of modulation are typically examined by measuring expression of the reporter genes (column 25, lines 41-59). In working examples, *Chanda* transfected HEK293 cells with a vector

construct comprising a nucleic acid encoding AP-1 operably linked to luciferase reporter gene, applying a candidate modulator (stimulator) of AP-1, and measuring reporter gene activity in response to the modulator (e.g. figure 2). *Chanda* teaches the vector for delivering the nucleic acid may be adenoviral vectors (column 34, lines 3-14). Although *Chanda* did not transfect an immunocyte in working examples, it was apparently known in the art that immunocytes are natural host cells for AP-1 as taught by *Chanda.*

Kikuchi supplemented *Chanda* by establishing the skilled in the art had reduced to use primary immunocyte for measuring AP-1 activity. *Kikuchi* teaches transfecting human peripheral blood monocytes with AP-1 reporter plasmid containing luciferase reporter gene operably linked to a promoter (see e.g. pages 746-7), administering clarithromycin or LPS stimulators, and measuring reporter gene activity to assess the effect of stimulators on IL-8 signal pathway and activation of AP-1 (e.g. figure 2). [Underlining added.]

Applicants respectfully traverse this rejection with respect to the amended claims. As stated above, "*Chanda* transfected HEK 293 cells with a vector construct." The Office Action acknowledged that *Chanda* did not teach transfecting immunocytes. The rejection relied on *Kikuchi* to remedy this acknowledged deficiency as quoted in the underlined passage above. Applicants respectfully submit that the statement: "*Kikuchi* supplemented *Chanda* by establishing the skilled in the art had reduced to use primary immunocyte for measuring AP-1 activity." represents a misunderstanding of *Kikuchi*. At page 747, column 1, under "*DNA transfection and luciferase assay" Kikuchi* actually teaches:

Individual plasmids, together with a *Renilla* luciferase expression plasmid [pRL-TK: an internal control to indicate the total cellular transcription level (Promega)], were cotransfected into THP-1 cells using the Effectene Transfection Reagent (Qiagen GmbH, Hilden, Germany). After 48 h, the cells were plated into a 96-well plate (8×10^5 cells per well) and exposed to LPS (0 or 1 mg/L) and clarithromycin (0 or 10 mg/L) in RPMI 1640 medium with 10% FCS. After 4 h, cells were harvested and the luciferase (i.e. firefly luciferase) activity and the *Renilla* luciferase activity were measured using the Dual·Luciferase reporter assay system (Promega). The Luciferase activity was

normalized by the *Renilla* luciferase activity to calculate the relative luciferase activity. [Underlining added.]

Applicants respectfully submit that *Kikuchi* teaches transfecting a THP-1 cell line and although mentioning "human peripheral monocytes" (See, e.g., page 747 column 1, line 2.) notably transfects only the cell line. This practice is as described in the instant specification. Use of primary cells is clearly avoided in the applied reference teachings. The applied references accordingly cannot properly be said to teach or suggest all the claim limitations especially as now clarified by explicit recitation of "a primary immunocyte" and also may be said to demonstrate a lack of expectation of success given that although primary cells were used in some experiments described in *Kikuchi,* only cell lines were transfected. Clearly the Office Action fails to establish a *prima facie* case of obviousness according to the procedure as set forth in the MPEP:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP §2143.

Kraal does not remedy these noted deficiencies in establishing a *prima facie* case of obviousness as *Kraal* is only applied as "establishing methods of identifying iDC was well known in the art". Accordingly, the combination of applied references cannot properly be said to have established a *prima facie* case of obviousness. Reconsideration and withdrawal of this rejection are respectfully requested.

Restriction

Applicants recognize the finality of the restriction requirement. However, in view of the amended claim set and remarks above, Applicants respectfully request rejoinder of all claims before issuance of a Notice of Allowance.

Conclusion

In view of the above amendments and remarks, Applicants respectfully request reconsideration and withdrawal of all pending rejections. Applicants respectfully submit that

the application is now in condition for allowance and request prompt issuance of a Notice of Allowance. Should the Examiner believe that anything further is desirable that might put the application in even better condition for allowance, the Examiner is requested to contact the undersigned at the telephone number listed below.

Fees

No fees not otherwise provided for are believed to be necessitated by the instant response. However, should this be in error, authorization is hereby given to charge Deposit Account no. 18-1982 for any underpayment, or to credit any overpayments.

Respectfully submitted,

/George S. Jones/
George S. Jones (Reg. No. 38,508)
Attorney for Applicant

sanofi-aventis U.S. Inc.
Patent Department
Route #202-206 / P.O. Box 6800
Bridgewater, NJ 08807-0800
Telephone (908) 231-**3776**
Telefax (908) 231-2626

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